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Evidence Report/Technology Assessment

Number 48

Cardiovascular Effects of Epinephrine in Hypertensive Dental Patients

Summary

Overview

About 24 percent of the U.S. adult population is hypertensive (that is, has high blood pressure), when hypertension is defined by a mean systolic blood pressure of 140 mm Hg or greater, a diastolic blood pressure of 90 mm Hg or greater, or use of prescription antihypertensive medication. Of this hypertensive population, 48 percent are untreated, 24 percent are successfully treated, and 28 percent are inadequately treated. Thus, hypertensive individuals, both controlled and uncontrolled, will represent a substantial proportion of a typical dental practice's adult patients.

Epinephrine is widely used as an additive in local anesthetics (typically in concentrations of 1:100,000) to improve the depth and duration of the anesthesia, as well as to reduce bleeding in the operative field. Epinephrine counteracts the anesthetic's localized vasodilator effects in subcutaneous and submucosal vessels, thereby reducing the risk of anesthetic toxicity by decreasing the rate of systemic absorption from the site of injection. Epinephrine is also impregnated in cotton cord that is inserted into the sulcus between a tooth and the surrounding gingiva, improving access for tooth preparation and allowing dental impression material to more readily flow into the sulcus to record details of teeth prepared for crowns. This use of epinephrine also constricts the blood supply to adjacent tissue, thereby permitting the impression to be secured without contamination by bleeding.

Despite these benefits, which may not be as readily achievable through use of non-epinephrine preparations, the clinical impact of cardiovascular and hemodynamic changes caused by the introduction of exogenous epinephrine makes its use among hypertensive individuals a controversial subject in dentistry. The added risks attributed to the use of epinephrine in hypertensive patients include:

- through the direct action of epinephrine—greater probability of acute hypertensive crisis (dangerously high blood pressure), angina pectoris and myocardial infarction, as well as cardiac arrthymias; and
- brought about by the interaction of epinephrine and some antihypertensive medications—acute hypertensive or hypotensive crisis.

Recommendations for the use of epinephrine in clinical dental practice are not in full agreement. Most recommendations advise caution in using local anesthetics with epinephrine in patients with hypertension . Some authors indicate that epinephrine is contraindicated in patients whose hypertension is controlled, but who are taking medications with known epinephrine interactions; other authors indicate that epinephrine use is acceptable with appropriate precautions and monitoring. Opinion is also divided about the use of epinephrine in patients whose hypertension is uncontrolled, with some authors cautioning against it, while others indicate that this practice is appropriate in most instances. Virtually all recommendations, including those of manufacturers, discourage the use of epinephrine-impregnated gingival retraction cord in patients with uncontrolled hypertension.

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Methods

The key question for this systematic review, undertaken by the Research Triangle Institute Evidence-based Research Center, in Research Triangle, NC, is stated as "What additional risks of adverse cardiovascular outcomes do epinephrine-containing local anesthetic solutions and epinephrine-impregnated gingival retraction cords represent for controlled and uncontrolled hypertensive individuals receiving dental treatment?" Because adverse events are relatively rare, the authors examined the literature for studies reporting changes in risk indicators for adverse events, as well as for adverse events themselves. The authors defined adverse events as headache, syncope (fainting), angina, hypertensive crisis, longer-term arrhythmia, cerebrovascular accident (stroke), and myocardial infarction. They considered risk indicators to include changes in blood pressure, heart rate, and stroke volume, and plasma epinephrine concentration, and electrocardiographic (EKG) disturbances including transient arrhythmias.

The authors conducted separate literature searches focusing on effects of epinephrine in anesthetic solutions and in gingival retraction cord. In both instances they searched MEDLINE initially, with additional searching conducted in EMBASE and the Cochrane Controlled Trials Register. No attempt was made to search the gray literature, i.e., dissertations, theses, unpublished studies, abstracts, industry reports, and other nontraditional sources. The authors limited the searches to English language reports. Subsequently, they examined reference lists of studies identified in these searches to include additional reports of possible interest. They identified 373 reports addressing the use of epinephrine-containing local anesthetics and 33 addressing epinephrine-impregnated gingival retraction cord. They then reviewed these studies for possible inclusion in the evidence table. The authors used essentially identical inclusion criteria in both reviews that addressed the inclusion and separate analysis of known hypertensive subjects, exposure to known concentrations of epinephrine through receipt of an intraoral injection or application of gingival retraction cord, recording of at least one cardiovascular or hemodynamic outcome, and a dental setting with dental treatment provided. The authors used independent dual review, and eventually identified six local anesthetic studies that met the criteria for inclusion. No retraction cord papers met the criteria because no studies included hypertensive subjects.

The authors abstracted data from the included studies directly into the evidence table. They did not meta-analyze the results because two of the studies reported no information describing variation about the mean. The authors rated the quality of each included study using a rating scale that assessed several elements of internal and external validity, including sample size, presence of a comparison group of normotensive subjects, use of control groups (without epinephrine), outcomes reported, measurement methods, statistical testing, determination of hypertensive status, and reporting issues. They then graded the strength of the combined evidence, using a three-category system. The evidence was considered to be good if the numbers of studies and subjects were large (10 or more studies, 500 or more subjects), the quality of the studies was generally high (median quality score of 70 or higher), the results of these studies were consistent, and taken together, the results were comprehensive with respect to risks examined. The evidence was considered to be fair if the numbers of studies and subjects were adequate overall (5 or more studies, 200 or more subjects), the quality of the studies was generally acceptable (median score of 55 or higher), the results of these studies were reasonably consistent, with inconsistencies reflected as quantitative rather than qualitative differences, and the principal known risks were adequately examined. The evidence was considered to be poor if the numbers of studies and/or subjects were small (fewer than 5 studies or 200 subjects), or the quality of the studies was generally low (median score of less than 55), or there were substantial inconsistencies in the results, or the risks examined among the studies did not represent a reasonably complete assessment of known risks.

Results

The six included studies comprised 325 subjects, of whom 177 were identified as hypertensive. Of these, 25 (14 percent) were identified as taking medication for control of hypertension. In all studies the local anesthetic involved was 2 percent lidocaine, and epinephrine concentrations were divided between 1:100,000 (n=3 studies) and 1:80,000 (n=3 studies). Quantities of anesthetic solution injected were reported in four studies, with means ranging from 2 ml to 4.5 ml. The outcomes examined in these studies consisted principally of systolic and diastolic blood pressures and heart rate. EKG recordings were collected in two studies. The dental procedure involved was tooth extraction in five of the six studies, and "minor oral surgery" in the sixth.

The results suggest that hypertensive subjects undergoing an extraction experience small increases in systolic blood pressure and heart rate associated with the use of a local

anesthetic containing epinephrine (4 mm Hg and 6 beats per minute [bpm], respectively). These increases associated with the use of epinephrine occur in addition to increases in systolic and diastolic blood pressure and heart rate associated with undergoing the procedure without epinephrine (11.7 and 3.3 mm Hg, and 4.7 bpm, respectively) that are larger for hypertensives than for normotensives. No adverse outcomes were reported among any of the subjects in the studies included in the review, and only one report of an adverse event associated with the use of epinephrine in local anesthetic in a hypertensive patient was identified in the literature.

The researchers rated the strength of the evidence as poor for describing additional risks among controlled and uncontrolled hypertensives due to epinephrine-containing local anesthetic solutions and gingival retraction cords. These ratings result from both the number of available studies and their quality. For outcomes of the administration of local anesthetic solutions containing epinephrine to patients taking medications for the control of hypertension, one study comprising 14 subjects and two medications was available. Two other studies included patients taking antihypertensive medications, but outcomes were not reported separately. No studies described outcomes of the use of gingival retraction cord either for hypertensive patients, or for those taking medications for the control of hypertension. There were five studies addressing outcomes of the use of epinephrine-containing anesthetic solutions in hypertensive patients. The strength of this evidence was rated as poor because the outcomes considered in the studies did not represent a reasonably complete assessment of risk indicators, and because transient effects in blood pressure and heart rate, the principal outcomes reported, might have remained undetected in three of five studies.

Future Research

Based on the available evidence, which suggests that adverse outcomes among hypertensive patients are infrequent and that hemodynamic outcomes, which may be viewed as risk indicators, reflect only minimal change, replication of existing studies does not represent an efficient method to further our knowledge of the risks for adverse cardiovascular outcomes associated with use of local anesthetics containing epinephrine. Rather, a large-scale descriptive study of adverse outcomes of the use of epinephrine-containing local anesthetics would seem to be indicated. A long-term protocol initiated in one or more large dental clinics that involves electronic capture of pre-existing cardiovascular diagnoses and medication status of all patients, together with information describing all adverse outcomes occurring during treatment could begin to quantify the magnitude of additional risk represented by the use of epinephrine in hypertensive dental patients with minimal outlay of effort and expense. Only if the results of such an investigation indicate that the added risk is greater than deemed acceptable would additional trials to develop more sensitive methods for identifying patients at increased risk be justified.

With respect to the use of epinephrine-impregnated gingival retraction cord, studies are needed to quantify the absorption of epinephrine from gingival tissues. The effects of time, tissue condition, cord construction, and epinephrine concentration on plasma concentration of epinephrine should be determined in these studies. Once a better understanding of the possible range of epinephrine concentrations is gained, the risks associated with the use of these cords in hypertensive patients can be evaluated. At present, a single human study reports absorption levels.

Availability of Full Report

The full evidence report from which this summary was derived was prepared for the Agency for Healthcare Research and Quality by the Research Triangle Institute–University of North Carolina Evidence-based Practice Center under contract No. 290-97-0011. A limited number of prepublication copies of this report are available free of charge from the AHRQ Publications Clearinghouse by calling 800-358-9295. Requestors should ask for Evidence Report/Technology Assessment No. 48, Cardiovascular Effects of Epinephrine on Hypertensive Dental Patients. The final report is expected to be available by late Spring 2002 (AHRQ Publication No. 02-E006). At that time, printed copies may be obtained.

Internet users will be able to access the report online through AHRQ's Web site at:
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